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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,807	02/27/2004	Benjamin Tjoa	NWBI135118	5631

26389 7590 01/06/2011

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EXAMINER	
JUEDES, AMY E	
ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
01/06/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

efiling@cojk.com

Office Action Summary	Application No.	Applicant(s)	
	10/789,807	TJOA ET AL.	
	Examiner	Art Unit	
	AMY E. JUEDES	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-29* is/are pending in the application.

4a) Of the above claim(s) *4-7, 10-12, 16, and 24-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,8,9,13-15 and 17-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and remarks, filed 11/12/10, are acknowledged.
Claims 1, 3, and 19-20 have been amended.
Claims 1 and 4-29 are pending.

2. Claims 4-7, 10-12, 16, and 24-29 stand withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.
Claims 1, 8-9, 13-15, and 17-23 are being acted upon.

3. IT is noted that claim 3 is indicated as cancelled. No claim text shall be presented for any claim in the claim listing with the status of "canceled ". Correction is required.

4. The rejection of the claims under 35 U.S.C. 102 is withdrawn in view of Applicant's amendment to the claims.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
Claims 1, 8-9, 13-15, and 17-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification provides insufficient guidance to differentiate immature dendritic cells having CD1a and decreased expression of CD14, from non-activated monocytic precursors, as broadly claimed.
As set forth previously, The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be

considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. With these teachings in mind, an enabling disclosure, commensurate in scope with the breadth of the claimed invention, is required.

The instant claims are drawn to a method of differentiating monocytic precursors into immature dendritic cells having decreased expression of CD14 and increased expression of CD1a comprising contacting non-activated monocytic precursors with GM-CSF in the absence of additional cytokines. The state of the art is such that obtaining immature dendritic cells with GM-CSF in the absence of additional cytokines is extremely unpredictable. For example, Chaperot et al. teach a method identical to that of the instant claims, including culturing the monocyte precursors in non-adherent bags, but fail to obtain CD1a+ immature dendritic cells after culture in GM-CSF in the absence of additional cytokines. Chaperot et al. teach isolating the monocytic precursors by various methods including cytapherisis, density gradient preparation, and negative selection (see page 1668, in particular), which are conditions disclosed by the instant specification as "non-activating". Likewise, Bernard et al., 1998 (of record) teach a method identical to that of the instant claims, including culturing in PFTE bags, but again fail to obtain immature dendritic cells with reduced CD14 expression by culture with GM-CSF in the absence of additional cytokines. Furthermore, Sallusto et al. (of record) culture monocytic precursors in the presence of a medium containing 10% serum along with GM-CSF alone, which as disclosed by the instant specification prevents tight adherence and activation of the cells. However, Sallusto et al. fail to obtain CD1a+ immature dendritic cells. While other references (i.e. Matera et al. and Kasinrerk al.) do obtain a population of CD1a+ cells displaying decreased expression of CD14 by culture in GM-CSF in the absence of additional cytokines, it is not readily apparent which factors are critical for successfully obtaining said cells compared to the methods of Sallusto et al, Bernard et al., or Chaperot et al. Thus, based on the extremely unpredictable nature of the art, the instant specification must provide a sufficient and enabling disclosure commensurate in scope with the instant claims.

The instant specification teaches that the critical factor in obtaining immature dendritic cells by culture with GM-CSF in the absence of additionally cytokines relates to the activation status of the monocytic precursors. The specification teaches that the monocytic precursors should be isolated and cultured in such a way as to prevent their activation. For example, the instant specification discloses that non-activated precursors can be obtained by inhibiting the tight adhesion of monocytic precursors to the culture surface. The specification discloses on page 6 that this can be accomplished by a using low avidity culture vessels, or by including a high concentration of animal serum in the culture. The instant specification further discloses various methods for isolating the monocytic

precursors such that they are non-activated, but the disclosed methods are the same as those taught in the prior art, including aphaeresis, centrifugation, or positive/negative selection. The instant specification further provides specific examples in which monocytic precursors are cultured with GM-CSF in the absence of additional cytokines to obtain CD1a+ immature dendritic cells. The examples disclose culturing the cells in low-avidity bags, or with a high concentration of serum protein. However, both Bernard et al. and Chaperot et al. have performed the method using a low avidity culture vessel and isolation of the cells using a non-activating method, and failed to obtain CD1a+ immature dendritic cells with reduced CD14 expression. Moreover, Sallusto et al. have cultured monocytic precursors with 10% serum, which according to the instant specification , should prevent tight adherence (and hence activation) of the precursors. However, Sallusto et al. also failed to obtain immature dendritic cells after culture in GM-CSF alone. Thus, it must be assumed that other critical factors are required to successfully perform the method of the instant claims, either in the cell isolation protocol or the cell culture conditions. Therefore, based on the unpredictability of the art, the instant specification does not provide sufficient guidance to enable one of skill in the art to obtain "non-activated" precursor as broadly claimed, that would result in a CD1a+ immature dendritic cell after culture with GM-CSF in the absence of additional cytokines.

Applicant's arguments filed 11/12/10 have been fully considered, but they are not persuasive.

Applicant argues that none of the cited references teach the same method as recited in the instant claims, and that the methods of Bernard et al. and Chaperot et al. must either begin with activated monocytic precursors, or the monocytes adhered to the bags during culture. Applicant notes that the skilled artisan would be able to alter the methods of Bernard et al. and Chaperot et al. using the teachings of the instant specification to obtain immature dendritic cells.

Bernard et al. and Chaperot et al. teach isolating monocytes by aphersis/cytapherisis and/or density centrifugation. The specification on pages 6-7 specifically disclosed that non-activated precursor cells can be isolated by aphaeresis and differential centrifugation, exactly as performed by Bernard et al. and Chaperot et al. Furthermore, Bernard et al. and Chaperot et al. teach culturing the precursors in hydrophobic PFTE bags, exactly as required by claim 8-9. Bernard et al. and Chaperot et al. specifically disclose the culture is an adherent free culture (see page 1672 of Chaperot et al. and page 17 of Bernard et al.). Thus, the references teach the exact method of the instant claims, but fail to obtain dendritic cells having no expression of CD14 and increased expression of CD1a. Applicant has not identified any specific teaching in the instant specification that that can be used to modify the method of

Bernard et al. or Chaperot et al. to obtain immature dendritic cells. Furthermore, even if the specification does disclose such a teaching, it is not part of the instant claims. The claims do not recite any method steps that differentiate them from the method of Bernard et al. and Chaperot et al. Thus, the claims are clearly missing essential steps that would enable the skilled artisan to obtain immature dendritic cells.

Applicant further argues that it is known from the specification that some PFTE bags can activate monocytic precursors, and that for example, high concentrations of an animal protein are required to prevent the activation of the precursor, as shown in Example 1.

Chaperot et al. teach culturing the monocytes in culture medium comprising autologous plasma, which comprises high concentration of animal proteins. Thus, using animal protein does not appear to be a factor that enables production of immature dendritic cells. Regardless, it is noted that the instant claims do not require the presence of animal proteins to prevent activation/adhesion, and in fact, claims specifically recite that adhesion/activation of the monocytes is inhibited by culture in a PFTE (i.e. Teflon) bag, exactly as performed in the cited references. Moreover, claim 13 specifically requires that the culture medium be serum free (i.e. encompassing culture in the absence of animal serum proteins). Thus, neither the specification or the claims define any method steps or elements that differentiate the claimed method from that taught by Chaperot et al. and Bernard et al. and that would enable the skilled artisan to produce immature dendritic cells.

6. No claim is allowed.

7. **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, whose telephone number is 571-272-4471. The examiner can normally be reached on 8am to 4:30pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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